

AMENDMENT TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently amended) An oxidation resistant engineered ribonuclease inhibitor (RI) variant of a ~~ribonuclease inhibitor~~ native RI, which ~~natively~~ has at least one pair of adjacent cysteine residues, the variant differing ~~in amino acid sequence~~ from the native RI by a substitution in form of the ribonuclease inhibitor only by having at least one ~~amino acid~~ cysteine of the at least one pair of ~~substitution in at least one of two~~ adjacent cysteine residues ~~present~~ in the native RI amino acid sequence ~~of the wild-type ribonuclease inhibitor~~, the ~~substitution~~ amino acid residue substituting for the cysteine residue ~~being an amino acid~~ residue not capable of forming a disulfide bond with an adjacent residue, the substituted ~~ribonuclease inhibitor~~ RI variant having a greater resistance to oxidation relative to the native RI, the substituted ~~ribonuclease inhibitor~~ RI variant retaining its specificity and binding affinity to ribonuclease, wherein the native RI is defined as SEQ ID NO: 2 or SEQ ID NO: 3.
2. (Currently amended) The ribonuclease inhibitor of claim 1, wherein ribonuclease inhibitor is a human ribonuclease inhibitor (SEQ ID NO:3) and the substituted cysteine residue is located in at least one of positions 95, 96, 329 and 330.
3. (Currently amended) The ribonuclease inhibitor of claim 1, wherein at least one of the adjacent cysteine residues is replaced with an alanine residue.
4. (Original) The ribonuclease inhibitor of claim 1, wherein the substitution in at least one of the cysteine residues inhibits the formation of a disulfide bond with an adjacent cysteine residue.

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5. (Original) The ribonuclease inhibitor of claim 1, wherein the mutant ribonuclease inhibitor is 10 to 15 fold more resistant to oxidative damage than the native human ribonuclease inhibitor.

6. (Original) The ribonuclease inhibitor of claim 1, wherein the ribonuclease is of the RNASE A superfamily.

7. (Original) The ribonuclease inhibitor of claim 1, wherein the modified ribonuclease inhibitor exhibits an in vitro inhibition of ribonucleolytic activity.

8. (Cancelled)

9. (Currently amended) A human ribonuclease inhibitor variant having at least one amino acid substitution in at least one of two adjacent cysteine residues present in the amino acid sequence of the wild-type ribonuclease inhibitor (SEQ ID NO:3), the substitution being an amino acid other than cysteine not capable of forming a disulfide bond with an adjacent amino acid residue, the remainder of the variant having the amino acid sequence of the wild-type ribonuclease inhibitor, the substituted ribonuclease inhibitor having a greater resistance to oxidation, the substituted ribonuclease inhibitor retaining the specificity and binding affinity to angiogenin of the wild-type human ribonuclease inhibitor.

10. (Previously presented) The ribonuclease inhibitor of claim 9, wherein the substituted cysteine residue is in at least one of positions 95, 96, 329, and 330.

11.-14. (Cancelled)

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15. (Currently amended) A human ribonuclease inhibitor variant comprising a protein having the amino acid sequence of native human ribonuclease inhibitor (SEQ ID NO:3) except for an amino acid substitution in at least two of the amino acids positions 95, 96, 329, and 330 of the native human ribonuclease inhibitor, each substitution being an alanine for a cysteine, the substituted ribonuclease inhibitor having a greater resistance to oxidation as compared to the wild-type human ribonuclease inhibitor, the substituted ribonuclease inhibitor retaining the specificity and binding affinity to angiogenin of the wild-type human ribonuclease inhibitor.

16. (currently amended) A human ribonuclease inhibitor variant comprising a protein having the amino acid sequence of SEQ ID NO:3, wherein the variant has an amino acid substitution in at least one of two adjacent cysteine residues, and wherein the substitution is an alanine to a cysteine.

17. (New) The ribonuclease inhibitor variant of claim 1, wherein ribonuclease inhibitor is a porcine ribonuclease inhibitor (SEQ ID NO:2) and the substituted cysteine residue is located in at least one of positions 324 and 325.